DISSERTATION ON

OUTCOME ANALYSIS OF THE USE OF ALLOGRAFTS IN SPINE FUSION SURGERY

Submitted for

M.S.DEGREE EXAMINATION
BRANCH II – ORTHOPAEDIC SURGERY

DEPARTMENT OF ORTHOPAEDIC SURGERY

MADRAS MEDICAL COLLEGE &
GOVERNMENT GENERAL HOSPITAL,

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI

MARCH 2009

BONAFIDE CERTIFICATE

This is to certify that this dissertation entitled "**Prospective study on the Outcome Analysis of the Use of Allografts in Spine Fusion Surgery**" *submitted by* ***Dr. C. DHANESH PRASAD*** *appearing for Part II, M.S. Branch II - Orthopaedics degree examination in March 2009 is a bonafide record of work done by him under my direct guidance and supervision in partial fulfilment of regulations of The Tamil Nadu Dr. M.G.R. Medical University, Chennai.*

I forward this to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

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ACKNOWLEDGEMENT

Any prospective study in a place as big as this Institution requires the support and guidance of a lot of people. It would only be appropriate if all the hours they have put in are properly remembered and acknowledged. My sincere thanks to **Dr**.**T.P KALANITI** **M.D**., Dean, Madras Medical College, for permitting the utilization of the resources and clinical material in this hospital.

I will forever be indebted to our Head of the Department and my Guide ***Padma Laureate*** **PROF. MAYIL VAHANAN NATARAJAN, M.S.Ortho., M.Ch., Ortho (Liverpool) ., D.Sc.,Ph.D., (Orthopaedic Oncology).** He has always been a constant source of inspiration with his advice and guiding me through the finer aspects of this study. Without him this study would not have been possible.

I express my profound thanks to my teacher **PROF. R.H.GOVARDHAN M.S.Ortho., D.Ortho.,** for his support, guidance and encouragement during the study.

I sincerely thank **PROF .V.THULASIRAMAN** **M.S.Ortho., D.Ortho.,** for his support during this study.

I am grateful to **PROF. S. SUBBIAH**., **M.S.Ortho., D.Ortho.,** for his valuable guidance.

I am grateful to **Dr**.**R.SUBBIAH**. **M.S.Ortho. D.Ortho,** Reader in Spine Surgery, for his support in this study.

I am profoundly thankful to **Dr.NALLI R UVARAJ,M.S. Ortho., D.Ortho., DNB Ortho.,** Reader in Spine Surgery, for all his valuable inputs to this study.

My sincere thanks to **Dr. R.SELVARAJ**., **M.S.Ortho., DNB Ortho** for his valuable guidance and useful inputs in the completion of this study.

I sincerely thank and **Dr. V. MAZHAVAN M.S. Ortho., D. Ortho and Dr.B.PASUPATHI MS ortho** for their constant support and guidance in during this study My Special thanks to **Dr. K. VELMURUGAN** for his constant encouragement and valuable guidance throughout the study.

I sincerely thank **Dr**.**T.R.RAMESH PANDIAN**, **Dr**.**ANTONY VIMALRAJ, Dr. N.B. THANMARAN, Dr. A. SHANMUGASUNDARAM, Dr. S. KARUNAKARAN, Dr. NALLI. R. GOPINATH, Dr. K.P.MANIMARAN, Dr. R. PRABHAKARAN, Dr N. MUTHALAGAN,Dr. SENTHIL SAILESH, Dr. SASIDHARAN** who have each been great mentors in their own way.

I must thank all my fellow post graduates, staff members of the Department of Orthopaedic Surgery, theatre staff and Anesthetists who have all chipped in with their support during the study.

Last but not the least I am immeasurably indebted to all our patients who consented and cooperated with this study.

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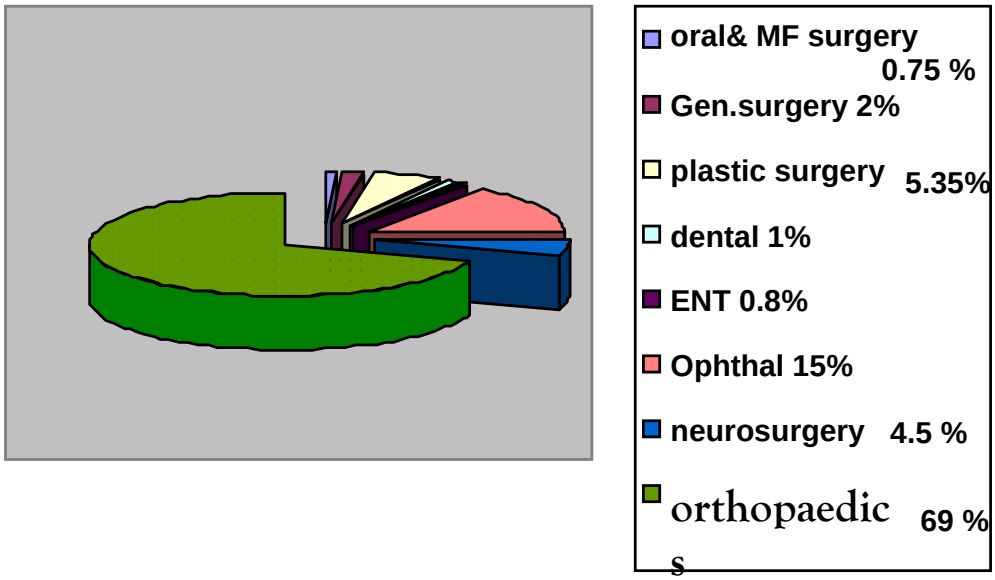
INTRODUCTION

Since time immemorial, replacement of man's organs have always found fascination amongst us. And among all replacements bone transplantations are the most widely performed.

"Bone is the most commonly transplanted tissue in the body than any other tissue or organ except blood".

Transplanted bone, tendon and ligaments are used extensively in orthopedics, neurosurgery, dental surgery and plastic surgery for procedures including repair of fractures and damage caused by illness and injury. . The application and the scope of allografts are the most in orthopaedics.

ALLOGRAFTS IN VARIOUS SURGICAL RECONSTRUCTIONS



Bone is a unique tissue in that its ability to regenerate is more predictable than any other tissue in the body. Bone is often destroyed by infection, tumor, trauma and implanted materials and has to be replaced to restore structure and function.

Bridging bone defects remains a challenging problem in orthopedic practice. The options available are

1. Vascularised autografts
2. Non Vascularised autografts
3. Custom made prosthesis
4. Biomaterials e.g. ceramics,
5. Allografts

Likewise ceramics are available from only in certain countries and very expensive. With the development of bone banks all over the world, bone allografts have become more readily available with high standards of safety for transplantation in patients.

Bone grafting is one of the most frequent operations performed. Autografts remain the gold standard as they are

osteoconductive as well as osteoinductive and have osteogenic cells.

Most of the time, amount of graft required is small and harvesting bone from the iliac crest and fibula is enough. When the graft requirement is larger in the massive defects or in children, where the autograft availability is small and harvesting can damage the open growth plates, the role of allografts comes into play. Autografting has many disadvantages like donor life morbidity, increased blood loss and increased operating time.

Complications involving the iliac bone-graft donor site are not uncommon. Although some of these complications may not be serious, they add to the patient's discomfort and prolong the convalescence. Complications secondary to graft removal from the ilium include

1. Major blood loss
2. Hematoma
3. Nerve injury (neuroma formation)
4. Severe pain (chronic pain)
5. Hernia
6. Cosmetic deformity
7. Fracture
8. Necessity for sacroiliac joint surgery

9. Pelvic instability
10. Hip subluxation
11. Gait disturbance
12. Peritoneal injury
13. Ureteral injury
14. Heterotopic bone formation
15. Infection

Allograft have been proved to be useful in massive defects, spinal fusions, large joint defects and reconstructive of bone tumors in spite of several short timings. Allografts have further extended the reconstruction abilities of surgeon and provide innovative option for biologic reconstruction with less patient morbidity.

The advantages of allografts are

1. Allografts can be stored for long time up to 6 years in case of freeze dried allografts and freeze dried demineralized allografts and 5 years for deep frozen allografts
2. It is cheaper than metallic implants
3. Easy to obtain and enormous availability of the graft
4. Decreased donor site morbidity

5. Biologic form of fixation (i.e., after incorporation allografted area becomes the quality of host bone)
6. Immunologic response is very minimal after storage hence there is no role of immunosuppressive drugs
7. Allografts of all dimensions can be prepared and used for deficient conditions
8. Soft tissues and ligament attachment are possible with allografts .
9. Can be stored for a long time
10. Shortened operating time
11. Good biologic bed for tendon and ligament reconstruction
12. Biological Reconstruction avoids long term complications of prostheses and ceramics (loosening etc)
13. Enormous savings in costs

APPLICATIONS OF ALLOGRAFTS

APPLICATIONS OF ALLOGRAFTS IN ORTHOPAEDICS

- Musculoskeletal Oncology

Reconstruction after Resection

  - Large structural allografts
  - Nonstructural allografts (morselized cancellous or cortico cancellous bone chips)

- Traumatic Bone Defect
  - Structural or non structural allograft
- Spinal surgery & Revision joint arthroplasty
  - Bone stock augmentation
  - Morcellized cancellous allografts
- Sports Medicine
  - Ligament reconstruction
  - Meniscal allograft
  - Osteochondral allograft

HISTORY

OF

ALLOGRAFTS

2500 years back Sushrutha used skin and bone allografts for nasal reconstruction.

In 1881 William McEwen of Glasgow performed the first successful bone allograft and initiated the modern practice of bone grafting. He successfully transferred segments of bone from a rachitic patient to the humerus of a three year old child suffering from osteomyelitis, and he performed rib graft to replace mandible.

Lexer in 1908 performed 29 allogenic whole joint transplantation. In 1914 phemister advocated bone grafting to enhance the process of creeping substitution. In 1935 – 1937 Bush and Wilson successfully stored allograft at 10 to 20^{o} C in New York.

Langer of Canada showed that reaction to allografts was greatly reduced by freezing the graft.

In 1956, Albee, the first orthopaedic surgeon started US bone bank in New York.

In 1960, Ethelene oxide sterilization has been used for bones.

In 1974, Radiation sterilization focused to be alterative for ETO sterilization on the grounds of safety and cost.

In 1978 Burchand et al described three patterns of allograft incorporation.

In 1983 W.W. Tomford suggested the use of glycerol and demethyl sulphoxide to maintain the viability of cartilage during freezing.

In 1989 M.R.Urist described the use of bone morphogenic protein.

In 1990 international atomic agency published guidelines for the radiation sterilization. In 1990 there was 30 tissue banks in USA and 31 tissue banks in Europe.

The first allograft transplantation in a Government Hospital in India was performed by Prof. Mayil Vahanan Natarajan in 2003 at the Govt. General Hospital, Chennai .

In 2005, the first bone bank in a Government Hospital in India was started in Government General Hospital, Chennai.

BIOLOGY & CORPORATION

OF

ALLOGRAFTS

A successful bone graft has to incorporate into the skeletal system of the host; graft incorporation depends on its size, structure, position, fixation and genetic composition. The role of the grafts in stimulating incorporation encompasses osteoconduction, osteoinduction and osteogenesis.

Osteoconduction and creeping substitution are the main mechanisms in the incorporation of allografts, Allografts act as a scaffold for in growth and it is referred as osteoconduction.

Graft Incorporation occurs in following Stages

1. Revascularisation

2. Graft resorption

3. Creeping substitution, new osteons laid over the Allograft.

4. Graft remodeling.

Revascularisation occurs by invasion of the capillary sprouts from the host bed and resorption of the old matrix follows with the investing osteoclasts & osteoblasts around the blood vessels that invade the graft.

After the laid of Osteons, callus formation ensures around the allografts serially which remodels in the course of time to ensure adequate incorporation.

Large Allografts may be incorporated in processing serial stress fractures that results in graft remodeling, periodically a region of stress concentration may microfracture followed by local remodeling. Later it proceeds to the whole length of the massive allografts. It takes a long time for the massive allografts to get incorporated into the skeletal system of the host.

Major type of allografts and their incorporation

1. **Allogenic Demineralised Bone matrix (DBM)**
2. **Morcellised (cancellous) allogenic bone**
3. **Massive Structural allograft**
    1. **Cortical**
    2. **Cortico-cancellous**
    3. **Osteochondral**
4. **Ligaments and Tendons**

TYPES OF ALLOGRAFTS

MAJOR TYPE OF ALLOGRAFTS

Demineralized Bone Matrix

It is formed after a mild acid extraction of cadaveric bone that removes the mineral phase, leaving the collagen, growth factors and non collagenous proteins that offer the intrinsic properties of osteoconduction and osteoinduction. It is powder that is mixed with a carrier. It is also available as gels, putties, pastes and fabric. It gets quickly revascularized and provides no structural support and moderately osteoinductive also. Within 1 hour, Implantation is followed by platelet aggregation, hematoma formation and inflammation characterized by migration of leucocytes.

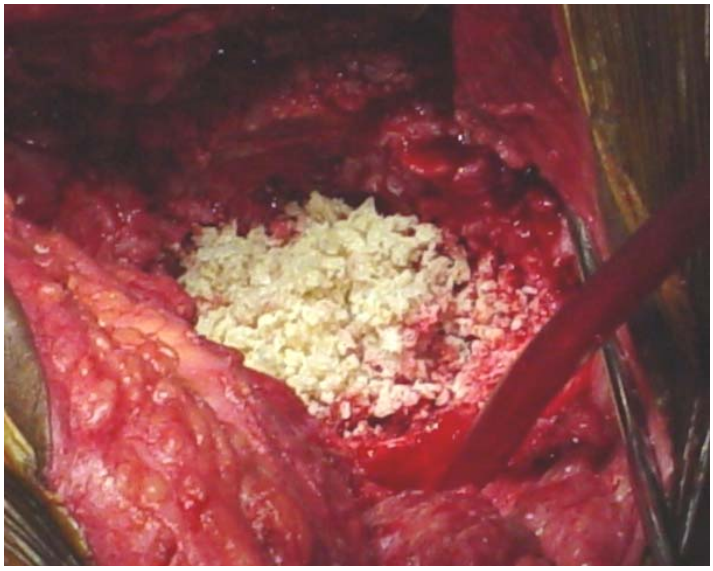
Fibroblast like mesenchymal cells undergone cellular differentiation into chondrocytes around 5 days. Chondrocytes produce cartilage matrix, which is mineralized. After 10-12 days vascular invasion with osteoblastic cells, new bone is formed opposite to the surface of the mineralized cartilage. Remodeling and replacement of these compound structures with new host bone ensues. With time, all the implanted DBM is resorbed and replaced with host bone.

DEMINERALISED BONE

MORCELLIZED AND CANCELLOUS ALLOGENIC BONE

Limited mechanical support and are osteoconductive only. Derived from either cancellous or cortical bone ranging from chips of sizes 0.5 to 3 mm diameter. They are characterized by an open, porous almost lattice like physical structure so that there is no physical improvement to the in growth of vessels.

The same stage of hemorrhage, inflammation, vascular ingrowth osteoid formation, remodeling and graft integration as in case of allografts take place. They are osteoconductive only and more resistant to compression. This may as weight bearing structures during the process of graft incorporation. They do not suffer the transient loss on mechanical strength that as resorption is not necessary for revascularisation.



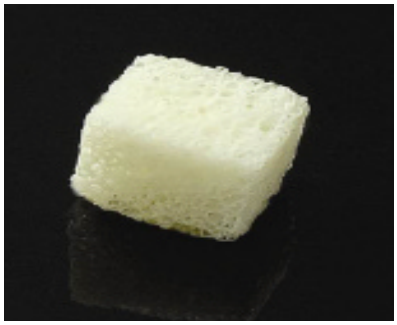
MASSIVE ALLOGRAFTS

The incorporation of massive allografts is a slow and incomplete process. Immune response is produced by the host even through the long storage in the deep freezer in order to reduce the immunogenicity. New bone formation from the periosteum of the host bone at the host graft junction is essential for the union at allograft host junction.

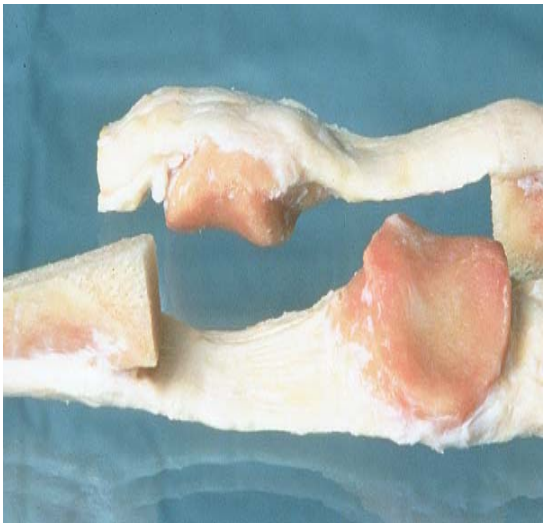
Creeping substitution and graft remodeling occurs in the slower phase and taken long time in achieving fusions. Optimizing the host - interface improves the functional outcome of massive bone allografts

CORTICOCANCELLOUS AND CORTICAL ALLOGRAFTS

They provide structural support and osteoconductive to a limited degree. The process of incorporation is slower than the DBM and cancellous allografts as resorption is necessary for revascu1arisation.



TENDO LIGAMENTOUS ALLOGRAFTS



ALLOGRAFT

IMMUNOLOGY

Organs and tissues transplanted into host incompatible animals or humans will induce an immune response. There is substantial evidence that bone, like other allogenic tissues, also induces such a response as a result of the recognition of a variety of potential alloantigens by the host's immune system. These antigens are capable of stimulating the full range of immune activities including cellular responses, antibodies and cytokine release.

IMMUNOLOGICAL COMPONENTS

Bone is a complex tissue comprised of many constituents capable of acting as sources of antigen. These include the non-cellular antigens of the extra cellular matrix such as collagen together with non-collagenous proteins (proteoglycans, glycoprotiens, etc.) as well as cells that express the major histocompatibility antigens. The primary cause of the host immune response in bone allograft transplantation are the cells of the bone marrow, primarily leukocytes. Reduction or removal of such cells by processing, freezing, freeze-drying or irradiation

reduces these cellular elements and thus lowers the likelihood of an immune response.

Several studies have demonstrated that after transplantation of frozen bone or soft tissue grafts that an immune response is generated causing antibody formation in up to 75% of the patients. This does seem to affect the outcome of massive bone transplantation. For tendon allografts it does not seem to have clinical importance. Transplantation of freeze-dried grafts does not cause antibody formation. Freezing and freeze-drying procedures decrease the antigenicity of bone. **Irradiation of bone not only sterilizes the bone but also destroys its antigenicity**.

HISTOCOMPATIBILITY MATCHING

Experimental results shows that matching does reduce immunogenicity and improves the outcome of bone allografts. However, the fact that the tissue transplanted after irradiation is only inert bone with minimal tissue antigenicity precludes the need for HLA matching as also the need for pre or post transplantation immunosuppressive **therapy**. Potential benefits in clinical practice which were initially unresolved have all been now proven.

PRESERVATION

The three most commonly used preservation methods are

1. **Deep-freezing - -80degree – 5years**
2. **Freeze-drying (Lyophilization) - -20degree –6 months**
3. **Cryo preservation – -160 degree**

FRESH FROZEN ALLOGRAFT (DEEP FREEZING)

In this method the graft is collected and frozen slowly in two steps; first to -20 degree Celsius for 8 hours, followed by freezing to -80 degree Celsius in order to stop all enzymatic activity. Allografts can be preserved by deep-freezing up to 5 years. Advantages of deep freezing are

1. Long bones such as femur and tibia are stored as fresh frozen allografts.
2. reduces the immunogenicity of the allografts,
3. Fresh frozen bone has got superior strength

Disadvantages are

1. High cost of operation of the freezers
2. Requires regular monitoring of the temperature of the freezer.

FREEZE DRYING (freeze dried allografts)

Freeze drying on lyophilisation is a process in which frozen bone is dehydrated by sublimation. Tissue moisture passes directly from the solid phase to the vapor phase and is converted to ice on the condenser of the freeze nitrogen.

A vaccum is maintained in the freeze dryer during the process, ensuring that bottles of bone allografts are sterilely sealed.This process allows tissue to maintained at room temperature for at least years or as long as the vaccum, seals remain unbroken.

Advantages of freeze-drying are

1. It can be kept at room temperature so storage made easy and cheap.
2. Reduced antigenicity as compared to deep freezing.
3. Transfer of disease is likely

Disadvantages are

1. Decreased torsional and bending strength of cortical grafts.
2. Not a suitable technique to preserve long bones.
3. It should be reconstituted by immersion in normal saline before use

CRYOPRESERVATION

The lower the temperature the greater the reduction of molecular activity, including enzymatic activity. At -160 degree Celsius the temperature of the liquid nitrogen, essentially all-molecular action is stopped and tissue can be stored indefinitely.

By cryopreservation allografts can be stored for life. Most of the bone banks in the world don’t prefer the cryopreservatives due to

its high cost and

4. Electrical deep freezer is as effective as liquid nitrogen preservation.
5. Rapid turn over of tissue makes it unnecessarily to store them indefinitely.
6. Liquid nitrogen may increase the brittleness of bone due to immediate crystallization of water that occurs upon rapid exposure to very low temperature.

STERLIZATION

The implantation of an allograft into the body carries with it an inherent risk of infection. It is extremely important to reduce the rate of infection by appropriate sterilization of the allografts. Sterilization has been defined as the process or act of inactivating all form of life, especially microorganisms. Aseptic procurement of allografts from donors who has little risk of infection in sterile operating rooms doesn't need a secondary sterilization. But allografts from the cadaveric bones need secondary sterilization wherever the procurement has taken place. The sterilization of allografts is an important inevitable process needs to be taken strictly in order to get the success of bone transplantation.

The commonly used sterilization methods are

1. Chemical like ethylene oxide
2. Radiation sterilisation using gamma rays 25 Kgy
3. WHO protocol is pasteurization at 60degree Celsius for 30 min followed by radiation for 25 Kgy for all grafts – cadaveric donors HIV protection
4. Autoclaving

Autoclaving

Bacteria are more readily killed by moist heat than dry heat. Steam kills bacteria by denaturing their protein. 121 degree Celsius for 15 to 20 minutes is the best method of steam sterilization. Autoclaving is not recommended by American Association Of Tissue Banks because it alters the structure of protein and alters the bone strength.

Ethylene oxide

Ethylene oxide is applied in a gaseous state in mixture with inert diluents such as carbon dioxide, Freon (dichioro difluro methane). After sterilization the residual ethylene oxide is replaced by flushing inert gas like carbon dioxide. Ethylene oxide sterilization of allografts also has lost its popularity because of its carcinogenic property of allografts.

Radiation sterilization

Two types of radiation are employed for sterilization namely ionizing radiation and non-ionising. Ultra violet rays are a non-ionising radiation most effective at 253.7 micron wavelength. It is mainly used for surface sterilization as it has very low penetration. Ionizing radiation includes high energy electrons generated from accelerated electro magnetic rays such as gamma rays emitted by radioisotope Cobalt60 and Caesium

137 and X-rays generated by X-ray machine. Ionizing radiation kills all types of microorganisms through the ionization process and usually has enough energy for useful penetration into solids and liquids of tissue. These rays can break and change the DNA strands. The treatment does not heat up tissue materials significantly and are widely used for industrial sterilization of the heat sensitive medical and laboratory products. Therefore this has gained popularity in sterilization of allografts.

Effect of preservation & sterilization:

Freezing bone decreases its tensile and compression strength by about 10 %. Freeze drying decreases torsional strength by about 5O% and compressive by 10%. Bending strength has been shown to be lowered up to 20% by each of its methods. Other physical modes of sterilization like autoclaving and pasteurization affects mechanical properties to greater extent. So that the graft can be used only where there is no need for structural support.

Radiation sterilization causes little change in the strength of structural allograft (3 mega rads of irradiation).

COMPLICATIONS

The following are the various complications of allografts.

1. Infection
2. Nonunion
3. Graft fracture
4. Transmission of infectious diseases
5. Graft resorption
6. Cartilage fragmentation
7. Implant failure

Infections are the most dreadful enemy for allograft reconstruction. Proper sterilization techniques, proper surgical techniques and good soft tissue cover will decrease the incidence of infection. Chemotherapy and radiotherapy will increase the incidence of infection by suppressing the immune mechanisms of the individual and revascularisation potential of the graft. Staphylococcus epidermidis is found to be the most common bacterial infection in the allografts.

Bone allografts have been implicated in transmitting tuberculosis, HIV, Hepatitis and bacterial infections to recipient. To prevent or at least minimize the risk of transmission of infectious disease, several steps are taken by surgeons and bone

banks. An important initial approach is to judiciously use bone allografts only when needed and to consider the use of auto grafts, alternative non human graft material or sterilized bone allografts whenever possible. However, the most important approach is exercised by the tissue bank donor coordinator who carefully obtains a medical and social history excluding those suspect to be at risk of HIV, hepatitis or other viral or bacterial infections.

Graft fracture and failure of graft incorporation are frequently found when massive allografts are used. This is not a problem with demineralised allografts, cancellous chips when used for fusion for spinal surgeries, cavity defects and impaction grafting in revision hip arthroplasty..

Graft resorption occur in some individuals to immune reactions of individual toward the graft. This occurs usually in patients frozen articular grafts. This is usually rare complication.

DISEASE TRANSMISSION WITH ALLOGRAFTS

Allografts are prone for disease transmission if the proper preventive steps and adherence to strict donor screening steps are not followed.

Bacterial and virus transmission have been reported with fresh frozen bone allografts. The disease transmission is rare in freeze dried bone allografts and demineralized freeze dried bone allografts.

The following bacterial and viral disease infectious agents have been reported in the use of allografts

1. Group A Streptococci
2. HIV virus
3. Hepatitis C virus
4. Hepatitis B virus
5. Treponema pallidum

Preventive Steps

Transmission of infection can be prevented by strict adherence to certain guideline with respect to procurement processing and sterilization of bone grafts

1. Procurement of the allografts is the most important step in preventing the transmission of infection. Following exclusion criteria should be considered while collecting the allografts.

a) High risk group donors

b) Testing for HIV / HCV / HBsAg / VDRL.

Always one should retest for HIV/ HCV antibodies after the donation to exclude donor during window period

c) Occult disease in donor on autopsy.

d) Donor bone tip should be tested for bacterial contamination at the time of procurement and final packaging. Tissue should be culture negative at that time of official packaging

e)Adherence to strict guidelines with the respect to processing and sterilization of the bone grafts.

RECENT ADVANCES

NEWER VISTAS IN BONE REPAIR IN THE 21ST CENTURY

As our understanding of the biology of bone formation keeps widening, surgeon and scientists have started exploring hitherto unknown “Grey Zones” in tissue engineering to enhance bone healing. The following are the options available to the 21st century Orthopaedic surgeon. (by the order of their introduction into use)

Bone Morphogenetic Proteins

They have the most osteoinductive potential amongst all bone substitutes. **Govender ,et al** reported faster union, fewer infections, and fewer secondary interventions in a study group treated with **12 mg** of **BMP-2** .

Ceramics - in the form of calcium phosphate pastes, putties.

BUT…..

- The use of milligram dosages when the body BMP levels are in the range of nanograms clearly poses concerns of dose safety.
- They are very expensive. Hence their role has to be very clearly outlined by more randomized trials to mandate their use in patients.

CELL BASED THERAPIES

STEM CELL THERAPY-

The use of injectable osteoprogenitor stem cells have been on trial recently. They are Mesenchymal Stem Cells(MSC) which are pluripotent cells with the capability to generate cells of the local environment's need.

GENE THERAPY

Modification of the patient's genes to " turn on" the osteoprogenitor cells.this is done in two methods.

- **In Vivo Method**- introducing an "altered" Adeno virus into the patient to stimulate/ modify the genes.
- **Ex Vivo method**- produce genetically "altered" stem cells for injection into the patient.

BUT…

- Multiple injections are necessary
- Expensive therapy.
- The potential unexplored possibility of uncontrolled cellular proliferation

AIM OF THE STUDY

To evaluate the rates of fusion of allografts and the analysis of their outcome in various spine fusion surgeries

MATERIALS

&

METHODS

The materials for this study was based on a prospective study conducted at the Department of Orthopaedics and Traumatology, Government General Hospital, Chennai from May 2006 till November 2008

Inclusion Criteria are

1. All vertebral fractures & fracture dislocations requiring stabilisation.
2. Spondylolysis,
3. Spondylolisthesis patients
4. Caries spine
5. Kyphoscoliosis correction

Exclusion criteria are

1. Age >55 yrs,
2. chronic nicotine users
3. diabetes mellitus
4. presence of any other co-morbid conditions affecting the microvasculature thereby influencing the rates of fusion.

IN THIS STUDY ……

As this study involves ethical issues with the transfer of biomaterial between patients, the need for a streamlined screening and documentation was felt.

The Institutional Ethical Committee clearance was obtained.

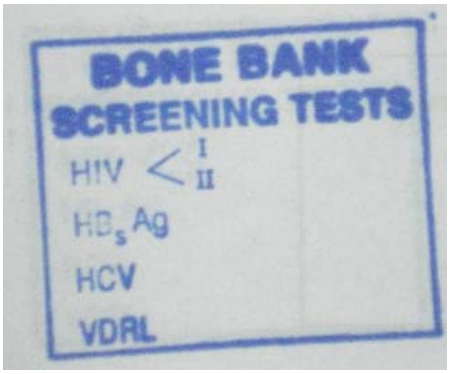
The following are the various aspects of allograft procurement and processing that was followed in our Bone Bank.

PROCUREMENT (Sterile Double Jar Technique)

Prior to procurement Donor consent was obtained in the prescribed format. Screening of the prospective donor for HIV I,II, HbSAg, HCV, VDRL, was carried out.

Femoral head (undiseased- # NoF) obtained from hip replacements are washed are normal saline and packed in pre-irradiated poly-ethylene TFC (PET) jars in sterile packages.

Screening forms



Pre-irradiated sterile PET jar with Double cover.

Packaged femoral head

ALLOGRAFT PROCESSING EQUIPMENTS AT OUR BONE BANK

LAMINAR AIR FLOW CHAMBER

ULTRASONIC BATH

ETO STERILISER

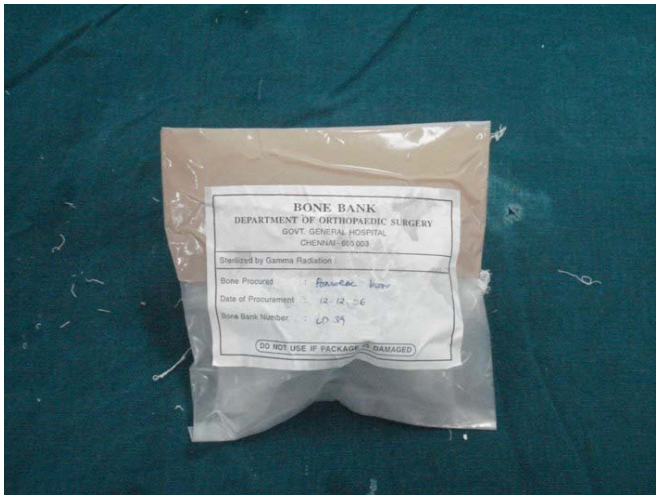
STORAGE - THE CRUX OF OUR BONE BANK

Both the pre- and post sterilization femoral heads are stored at -80* centigrade in Two Deep Freezers in the Bone Bank.

STERILISATION- GAMMA IRRADIATION

The allografts were irradiated upto 25KGy at The Kidwai Institute of Oncology, Bangalore. Irradiation has very little effects on the tensile strength of the allograft. Apart from femoral heads procured here, imported sterilized, long bone allografts were also preserved in the Deep Freezer.

DEEP FROZEN IRRADIATED ALLOGRAFT TRIPLE PACKS

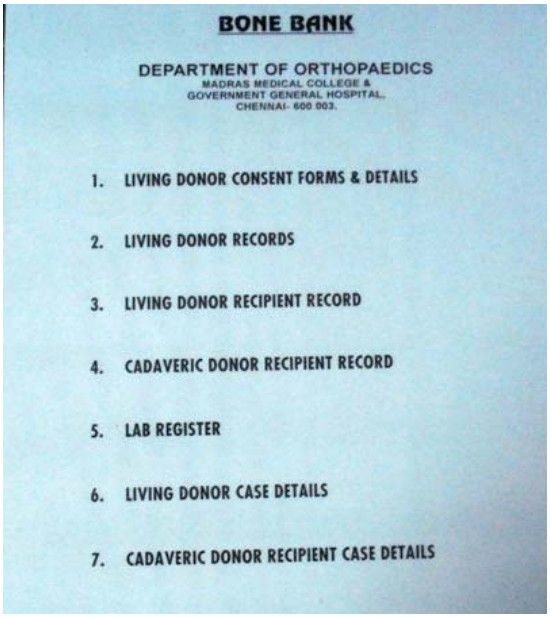


FRAMING A PROTOCOL:

Our own Bone Banking Protocol was framed based on International screening guidelines.

DOCUMENTATION:

At each step of the banking of allografts record maintenance was properly done and regularly updated. The records were also computerized.



BONE BANK PROTOCOL

Donor consent,screening

↓

Procurement of the bone (femoral heads, condyles, bone tendon grafts)

↓

Processing & Sterile packaging

↓

Donor screening after 3 months

negative ↙

positive ↘

graft discarded

Irradiation at 25 KGy

Preservation at -80 * (Deep Freezer)

↓

Proper patient selection.

Screening of the patient+ consent

Allograft implantation

Screening at 3 months post op.

IMPLANTATION

Pre operative recipient consent and screening were done.

Allograft preparation

Decartilaginising the femoral head, the cancellous core is morcellised into bits, and triple washed and RINSED to remove the fatty marrow. The morcellised bits are placed in an antibiotic solution (cefotaxime 1 gm) prior to grafting.

Graft bed preparation

Adequate preparation of the graft bed plays a long term role in the incorporation of allografts. The posterolateral mass of the dorsolumbar spine (transverse process, facet jts,) are shingled after soft tissue denudation. Placement of the

allograft on a properly prepared host bony bed was found to give better fusion rates among allografts.

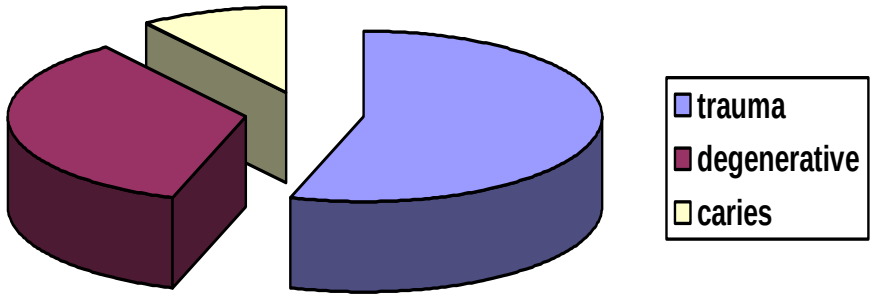
Adequacy of allografts was ensured to facilitate a solid bony mass formation.

TOTAL NO OF CASES : 20 patients

Male : female = 14 : 6

Mean age: 39.10 yrs (17 – 55 yrs)

Trauma	11 patients	55 %
Burst fracture	10	
Fracture dislocation	1	
Degenerative	7 patients	35 %
Degen. Spondylolisthesis	6	
Lytic spondylolisthesis	1	
Caries spine	2 patients	10 %
Dorsal	1	
Lumbar	1	



Investigations

After appropriate radiographs pre operative CT scan was a must to assess the canal dimensions and the anatomy of the Posterolateral structures.

Pre operative-

Bladder and bowel care as necessary given. Alpha beds were provided for prevention of pressure sores.

Intraoperative-

Anaesthesia – general Anaesthesia

Average duration of surgery- 1 hr 50 min

Avg time of graft preparation – 30 min

Implants used K fixator

Pedicle screws

Hartshill rectangles

POST OP PROTOCOL

a. drain removal after 48 hrs.
b. mobilization (sitting up) after drain removal with external brace.
c. Suture removal – 12 th post op day.
d. Back, bladder, bowel care taught.
e. External orthosis used for 8 weeks.
f. Advised review after 6 weeks
g. Screening of the patient at 3rd month.
h. Follow up every 3 m.
i. CT scan at each follow up

The Lenke's grading was used at each review session for assessment of fusion.

ILLUSTRATION OF CASES

CASE I

Perumal 30/M

L5S1 lytic spondylolisthesis with radiculopathy.

ORIF with **Kluger's Fixator**

Complications: nil

Type of graft implantation**: Allo- Autograft mixture.**

Lenke's grading @ maximum follow up (24m) – **Gr 1**

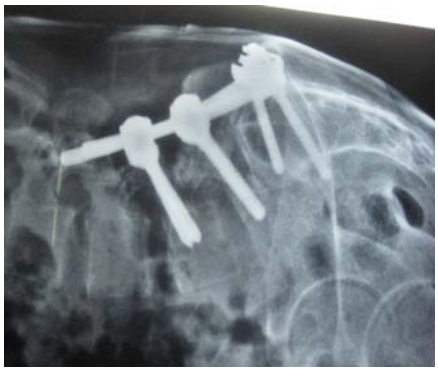
6m - Gr 2

9m - Gr 2

12m - Gr 1

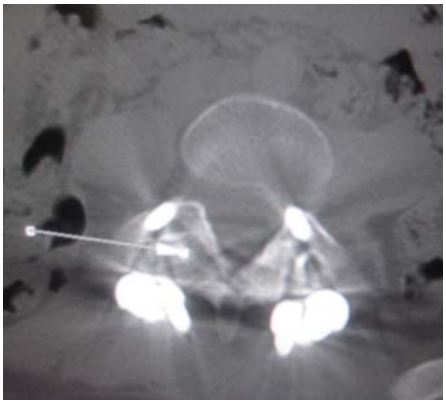
CASE I

PRE OPERATIVE **POST OPERATIVE**



CT scan at 9 m

CT scan at 16 m



CASE II

Rani 45/ F

L4-L5 degenerative spondylolisthesis

Decompression + insitu fusion **(No implant)**

Allograft type : **Pure allograft**

Complications: Nil

Lenke's grading at maximum follow up (17 m) **Gr 4**

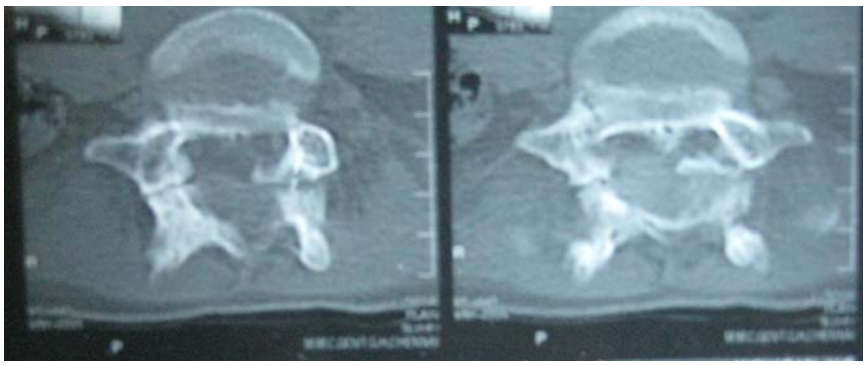
6m - Gr 3

9m - Gr 4

12m - Gr 4

Case II

CT at 16 months with loss of the allograft



CASE III

RAMA RAO 55/ M

D12 BURST FRACTURE + PARAPLEGIA

POSTERIOR STABILISATION (PEDICLE SCREWS & RODS)

TYPE OF ALLOGRAFT: **PURE ALLOGRAFT**

COMPLICATIONS: NIL

LENKE'S GRADING AT MAXIMUM FOLLOWUP (14m)- **Gr 4**

3m - Gr 3

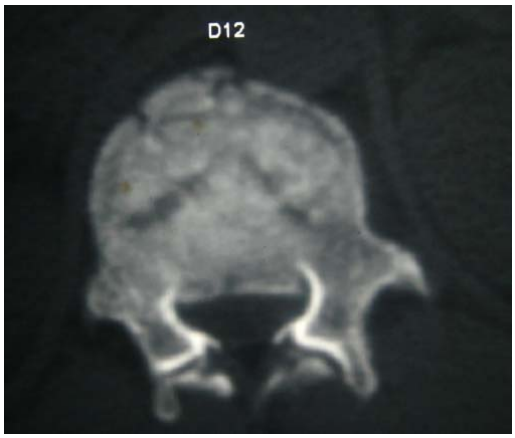
9m - Gr 4

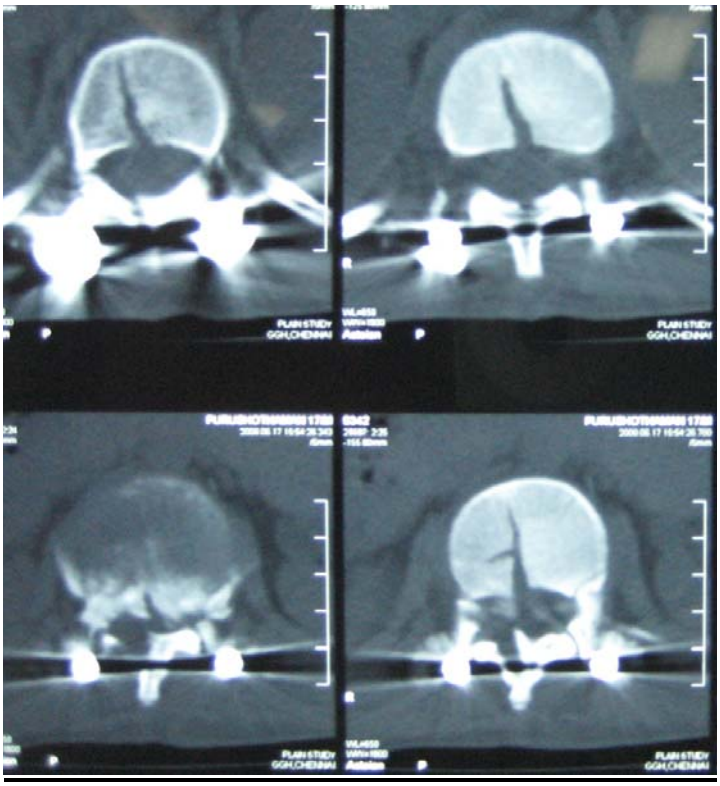
12m - Gr 4

CASE III

Pre operative

Post Operative


D12



CASE IV

VASANTH 18/M

L2 FRACTURE + PARAPLEGIA

POSTERIOR STABILISATION (PEDICLE SCREWS & RODS).

TYPE OF ALLOGRAFT : **PURE ALLOGRAFT**

LENKE'S GRADING AT MAX. FOLLOW UP - **Gr 2**

3m - Gr 3

6m - Gr 3

10m - Gr 2

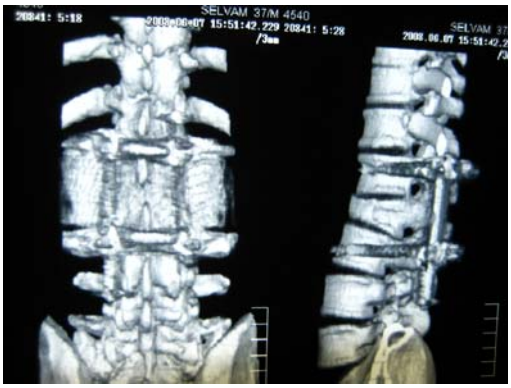
COMPLICATIONS: NIL

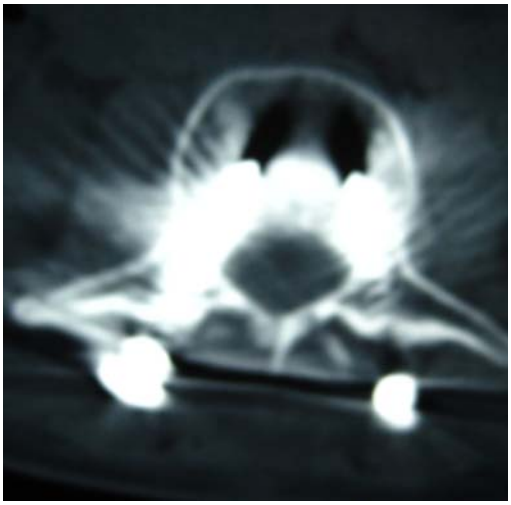
CASE IV

PRE OPERATIVE

POST OPERATIVE

CT Scan at 10 m





CASE V

SABANA BASHIR 51/F

L5 S1 DEGEN. SPONDYLOLISTHESIS + RADICULOPATHY

ORIF + PEDICLE SCREWS

TYPE OF GRAFT:

RT SIDE – PURE ALLOGRAFT

LT SIDE - PURE AUTOGRAFT

COMPLICATIONS: NIL

LENKE'S GRADE AT MAX. FOLLOW UP –

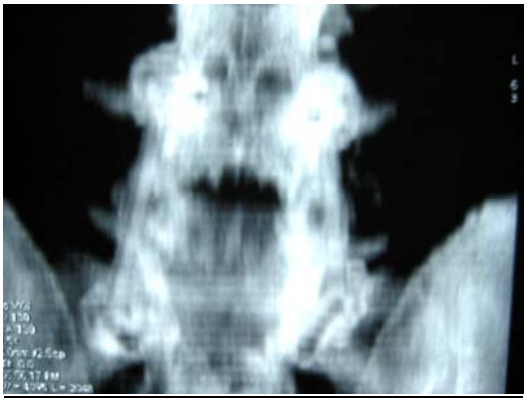
RT SIDE – Gr 3

LT SIDE - Gr 2

CASE V

Pre operative **Post operative**

Better fusion seen with autografts on the left



CT scan at 7 months

RESULTS

Follow up

At every follow up CT scan was taken to assess the radiological level of fusion.

Maximum follow up: 24 months

Minimum follow up : 7 months

Mean follow up : 11 months

No. of cases lost to follow up : 3 patients

(1 pt post discharge + 2 pts after one year of follow up)

No . of house visits done : 2

Assessment of fusion was done using the Lenke's fusion grading

LENKE'S GRADING OF FUSION

GRADE 1 Solid, big trabeculated fusions bilaterally(definitely solid)

GRADE 2 Solid, big fusion mass unilaterally with a small fusion mass on the contralateral aspect (possibly solid)

GRADE 3 Small, thin fusion masses bilaterally with apparent crack (probably not solid)

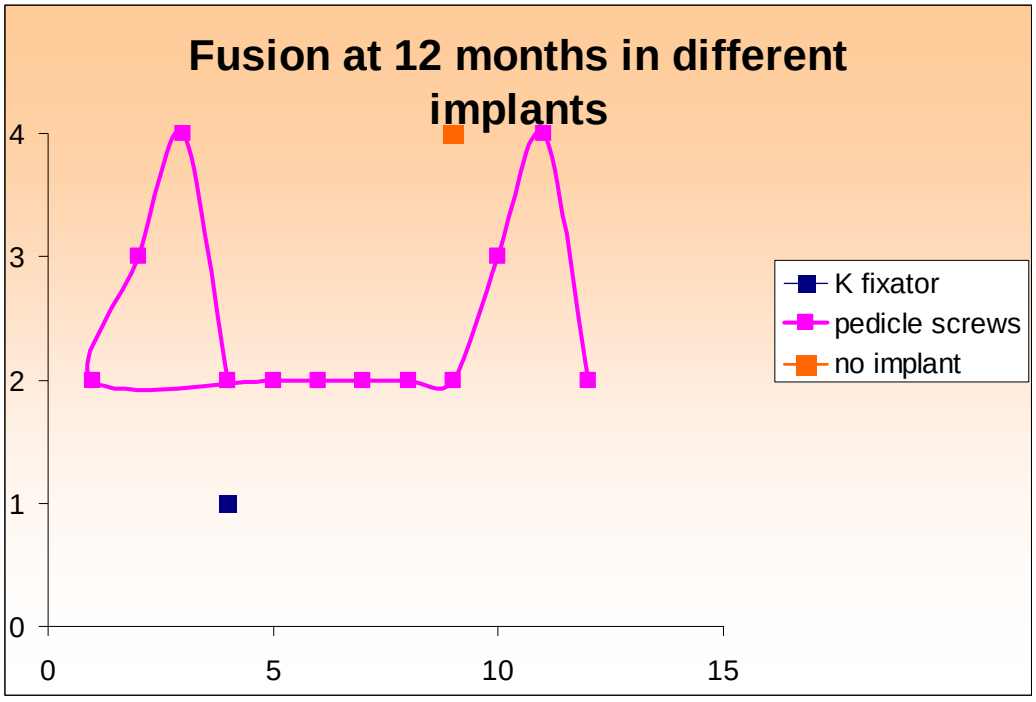
GRADE 4 Graft resorption bilaterally or fusion mass with an obvious bilateral pseudarthrosis (definitely not solid).

Maximal fusion achieved was Gr 1 **Minimal fusion was - Gr 4**

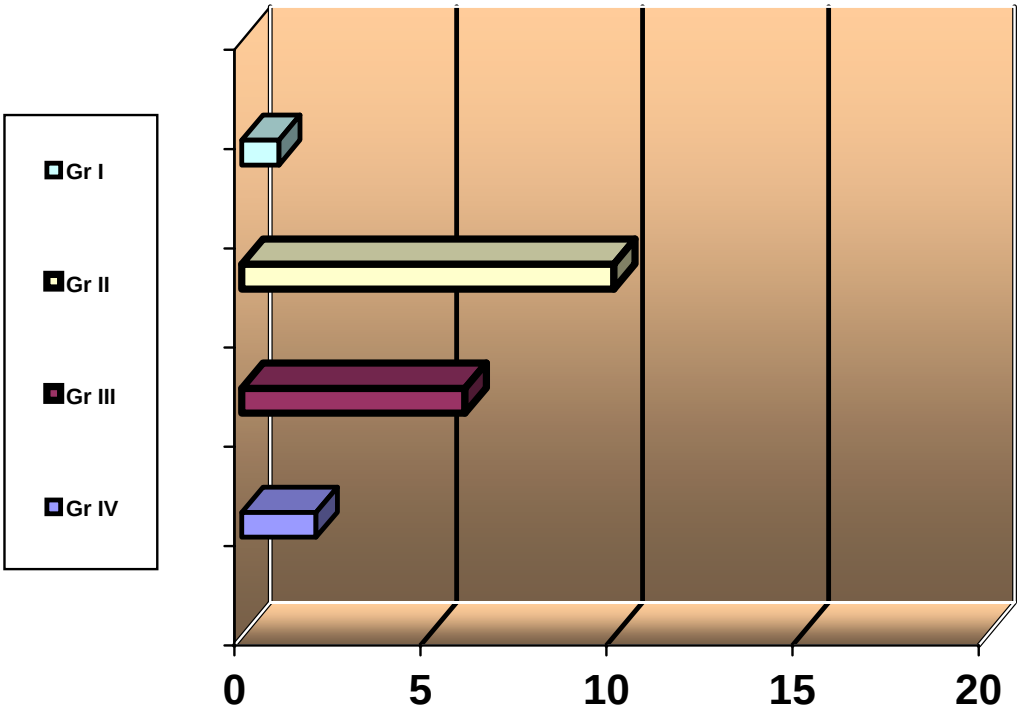
Type of graft	No. of pts	Max. Lenke's grading	Time taken	Min. grade achieved
Pure allograft	16	Gr. 2	12 m	Gr 4
Allo- Auto mixture	3	Gr. 1	12 m	Gr 2
Pt. no 18 Rt side – allograft Lt side - autograft		Gr. 3 Gr. 2	@ 7 m	

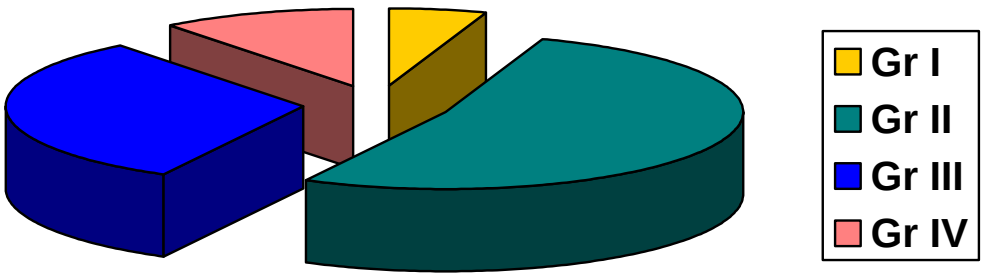
Type of implant	No. of pts	Max. Lenke's grading	Time taken	Min. grade achieved
K fixator	1	Gr. 1	12 m	
Pedicle screws	16	Gr. 2	10 m	Gr 4 (improper fixn)
No implants (in situ fusion)	1	Gr. 4 (graft resorption)	16 m	

Lenke's grading	No.of patients	Achieved at	Max follow up	Percent
Gr 1	1	12 m	24 m	5 %
Gr 2	10	12 m avg	16 m	50 %
Gr 3	6		10 m	30 %
Gr 4	2	@ 12m	16 m	10 %


Fusion at 12 months in different implants
4
3
2
1
0
0
5
10
15
K fixator
pedicle screws
no implant

OVER ALL FUSION





ANALYSIS OF RESULTS

Grade 2 fusion levels were considered as reasonably enough to take the load shared by the implant off. This level of fusion was achieved in 10 cases. Grade one fusion was seen in one case.

In order to compare the fusion rates with autograft added for osteo-induction 3 patients were embedded with auto – allograft mixture . They showed gr 2 fusion at 9m .

Neurological recovery was not a criteria in our evaluation.

Stability of fixation was an important criteria

Two cases of graft resorption were seen in those without implants or with improper, unstable fixation.One patient (L5S1 listhesis) had no implants, with decompression and in situ allografting. Though patient is symptom free, there was complete resorption of the allograft on the follow up CT at 16 months.

In one case(Case 18) of spondylolisthesis allograft were packed on the rt side with autograft on the left side. At 7 months follow up there was Grade 2 fusion at the autograft side while the allograft side showed Gr 3 patchy fusion, thereby demonstrating the slower fusion rates with allografts.

The mean period for achieving gr 2 fusion was 12 months.

There were **no allograft associated complications** like:

- Post op wound infection
- Graft rejection reactions.(manifesting as sterile discharges)
- Transmission of diseases

DISCUSSION

Allografting is a revolutionary procedure in the treatment of patients. To obtain a solid fusion in complex spinal problems, surgeons face both mechanical and biological difficulties. 4 factors affect the fusion of grafts in spinal fusion surgeries. They are:

- Osteogeneic potential
- Osteoinductivity
- Osteoconductivity
- Vascularity of the bed

With allografts only osteoconduction is possible, therefore their use being to predominantly augment the quantity of the graft. Hence also the importance of preserving the bed vascularity & ensuring proper preparation. Also a long segment of diseased spine or deviation from the mechanical advantages, such as a flat back or scoliosis, compromises the fusion rate when spinal fusion is attempted.

[Cummine et al. reported 59 patients who had pseudarthrosis status post-spinal fusion for scoliosis.The fusion rate was only 65%.]

[Lauerman et al. reported 51 patients with 63 pseudarthrose after posterior spinal fusion for idiopathic scoliosis. 56% had more than one level of pseudarthrosis. 40% of pseudarthrosis were in the lumbar spine.]

[Raney et al. found 53% of pseudarthrosis in 66 patients had underlying metabolic conditions such as osteoporosis, malabsorption syndrome, phosphate depletion secondary to antacid use, vitamin D abnormality or excessive tobacco or alcohol consumption.]

In our series the need to eliminate such factors predisposing to pseudarthrosis was felt. Hence exclusion criteria were framed regarding extremes of age (age >55 yrs), general nutritional status, metabolic bone disorders, history of previous spine surgery and other co-morbid conditions

It has been accepted that autogenous bone graft is preferable in both posterior and anterior fusion; however, often the amount of such bone graft is not enough either because it has been harvested from previous surgery or multiple levels of surgery are indicated.

Kozak et al. in 1994,[7] described the technique of anterior interbody fusion by using a femoral ring allograft packed with autogenous chip grafts to provide a strong construction to support the

spine anteriorly. The authors emphasized the preparation of the vertebral end plates as an essential technique.

In our series, 2 cases(caries spine) of anterior interbody fusion with femoral cortical ring allograft with autograft packing produced grade II Lenke's fusion at 12 m follow up. The slower rate of graft incorporation could be attributed to:

- delay in incorporation of the **cortical** bone of the femoral ring allograft (though the purpose of the autograft pack was solely to increase the rate and chance of fusion of the interbody graft)
- the presence of an infective foci at the site of fusion(caries)
- higher biomechanical loads in the dorso lumbar spine.

These 2 cases would only be a representation but cannot be compared to Kozak's series.[7]

An, Toth, and Lynch (1995) in their study have compared the rates of fusion of pure autografts, pure allografts , allo- autograft mixtures in spinal surgery fusion. Their results show that rate of fusion is the maximum with pure autografts followed by mixture grafts. Pure allografts have been shown to have the slowest rates of fusion. They have also been associated with the most no. of complications like pseudarthrosis, fusion fracture.[3]

Similar results were obtained with our study where 3 cases with allo-auto graft mixtures provided faster and better fusion results (grade 2 at a mean time of 9 months).

Nather ,Thambiah in 1996 have shown nearly 60 % fusion rateswith pure allografts, but justify their lower fusion rates with their contention that fusion of allografts though delayed, it was useful in older patients with porotic Iliac crests unsuitable for autograft harvesting.[4]

In our study the use of allografts in degenerative spinal diseases has provided good fusion (50%) . This fusion was Gr 2 at 12 m follow up. These patients need further follow up to assess the time required for Gr 1 fusion levels to be achieved.

In anterior fusion, the allograft, especially cortical bone of the femoral ring, required a considerable time before the full incorporation of the graft would take place. Kozak's was a larger series with purely anterior ring allografts for fusion. It appeared that at least 18 months is required before the majority of the grafts would be fully incorporated to the host bone.

One case in this study had a persistent radiolucent line at the interface between the graft and the shingled posterolateral surface.

The following is the analysis of the primary reference articles in comparison with this study

Nather & Thambiah	1996	60% fusion rates with allografts In degenerative cases. Failure of fusion noted in cases with Hartshill fixation.
Kozak	1995	97% fusion with femur allograft in ALIF
An, Toth	1995	Allo- auto mix provided 50% faster fusion than pure allografts
This study	2008	50% fusion rates with allo- auto mix. Implant stability plays major role in fusion rates Longer time (12m for Gr 2) required for fusion than autografts. Needs prolonged external orthoses for better results.

CONCLUSION

Bone autografting remains the most effective grafting material as it provides all the 4 essentials of bone regeneration. However the shortcomings of large harvesting and its associated morbidity provides us the scope for other alternatives. Among these alternatives allografts are the most inexpensive, most readily available option.

The attainment of solid bone fusion is multifactorial. There is a race between bone resorption and new formation in seeking to create a new fusion mass which can withstand mechanical loads. The following are the various conclusions regarding the multiple factors that governed allograft fusion in this study.

Deep Frozen Irradiated allografts have the maximum retention of their strength and structure.

There was **NO infection** during the use of these Irradiated allografts.

In anterior fusion the allograft, especially cortical bone of the femoral ring, required a considerable time before the full incorporation of the graft would take place. It appeared that at least **18 months** is required before the majority of the grafts would be fully incorporated to the host bone.

Another major conclusion was regarding **External Bracing** post operatively. In properly selected patients with extended external post operative immobilization the rates of fusion of allografts are better .

The **stability of the implant** as a factor for fusion needs to be stressed. Faster rates of fusion were seen in the more stable spine. The best result (Gr I) was achieved with a Klueger fixator.

The **quality and the quantity** of the allografts. With allografts there is everlasting quantity and mixing of minimal quantity of autografts provides the osteoinductive impetus to achieve faster fusion. Meticulous bed preparation yielded good results

Allografts are definitely a boon in the **older age group** with osteoporotic iliac crests.

Thus allografts are a definite solution for the problem of large bone harvests. Based on the review of our literature we conclude that bone allografts are a reliable and inexpensive alternative to autografts in spine fusion surgery.

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PROFORMA

OUTCOME ANALYSIS OF THE USE ALLOGRAFTS IN SPINE FUSION SURGERIES

CASE PROFORMA

CASE NO :

UNIT :

NAME	:	D.O.A	:
AGE	:	D.O.INJURY	:
SEX	:	D.O.S	:
I.P.NO.	:	D.O.D	:
ADDRESS	:	MODE OF INJURY	:

DIAGNOSIS :

PROCEDURE :

COMORBID FACTORS:

CONSENT FOR PARTICIPATION:

PREOPERATIVE SCREENING:

NEUROLOGY ON ADMISSION :

RADIOLOGICAL FINDINGS :

X ray :

CT :

SURGERY DETAILS

PROCEDURE :

ANAESTHESIA : POSITION :

APPROACH :

DURATION : BLOOD LOSS :

INSTRUMENTATION :

ALLOGRAFT DETAILS

TYPE OF ALLOGRAFT:

DONOR NO & SCREENING:

MODE OF STERILISATION:

STORAGE :

PREPARATION:

GRAFT IMPLANTATION**:**

POST OPERATIVE PERIOD

DRAIN REMOVAL:

INFECTION :

STERILE DISCHARGE:

POST OP NEUROLOGY:

POST OP RADIOLOGY :

PHYSIOTHERAPY AND REHABILITATION :

DISCHARGED ON:

FOLLOW UP with LENKE' S grading

ANNEXURES

ANNEXURE II

BONE BANK DONOR CONSENT FORM

ANNEXURE III

PATIENT CONSENT FORM

ANNEXURE IV

RECIPIENT RECORD

MASTER CHART

No	Name	Age Sex	I.P.no	Diagnosis	Neurology	D.o.S	Procedure	Allograft Details Donor	recipient	Compln Infecn	Follow up – Lenke's grading 3m 6m 9m 12 (max)			
1.	Chandran	55/M	801168	D9-10 caries spine	paraplegia	09.06.06	Ant.decomp+ tibial cort. Ring allograft+ autograft pack	LSAG 35	LR 18	nil				2 L
2	Malliga	45/F	794737	L3 caries spine	L/L 4/5	16.6.06	Ant.decomp+ fem ring allograft + autograft pack	LSAG 37	LR 19	nil				2 L
3	Perumal	30/M	802078	L5S1 listhesis	radiculopathy	20.8.06	ORIF + K fixator	LD 22	LR21	nil				1 (24 m)
4	Rani	45/F	001735	L4-5 listhesis	radiculopathy	12.4.07	Decompression + in situ fusion	LD23, 24	LR 23	nil				4 (17m)
5	Angammal	50/F	031785	L5S1 listhesis	radiculopathy	23.5.07	ORIF + Pedicle screws	LD25, 26	LR 24	nil				2 (16m)
6	Punniakodi	50/M	27799	D10 # disloc	L/L 2/5	24.5.07	Post.stabilisation + pedicle screws	LD27, 28	LR25	nil				2 (16m)
7	Murugan	32/M	032812	D12#	L/L 2/5	30.5.07	Post.stabilisation+ pedicle screws	LD29, 30	LR26	nil				2 (12m)
8	Senthilkumar	30/M	33824	L1 burst#	paraplegia	30.5.07	Post.stabilisation + pedicle screws	LD31-32	LR27	nil				2 (17m)
9	Kumar	40/M	34814	L5S1 listhesis	radiculopathy	12.6.07	ORIF + pedicle screws	LD 33	LR 28	nil				2 (16m)
10.	Diwan	37/M	34902	# D10 dislocn	L/L 1/5		ORIF + post.Stabil ped screws	LD 21	LR 20	nil				2 (16 m)
11	Sakthivel	31/M	34962	L1,L2 #	Paraplegia	28.6.07	Post.stabilisation + pedicle screws	LD 34	LR 29	nil			2	(14m)
12	Ramarao	55/M	11802	D12 burst#	paraplegia	08.1.08	Post.stabilisation +	LD35	LR30	nil			4	

							pedicle screws							(10m)
13	Pakkiri	50/M	12069	D4 burst#	paraplegia	15.1.08	Post.stabilisation + pedicle screws	LD36	LR31	nil				LOST
14	Gnanasekar	25/M	12576	L1 burst#	No deficit	15.1.08	Post.stabilisation + pedicle screws	LD 37	LR32	nil			3	(10 m)
15	Vasanth	18/M	12118	L2 #	paraplegia	16.1.08	Post.stabilisation + pedicle screws	LD 38	LR33	nil			2	(10 m)
16	Raja	45/M	12312	D11 burst #	paraplegia	20.1.08	Post.stabilisation + pedicle screws	LD 39	LR34	nil			3	(10 m)
17	Purushotaman	17/M	14224	L1-2 #	L/L 3/5	05.03.08	Post.stabilisation + pedicle screws	LD40, 41	LR 36	nil		3		(7 m)
18	Vasantha	40/F	14468	L5S1 listhesis	radiculopathy	12.3.08	ORIF + pedicle screws	LD46, 47	LR 37	nil		3		(7 m)
19	Sabana bashir	51/F	15110	L4L5 listhesis	radiculopathy	20.3.08	ORIF + pedicle screws	LD57, 58	LR39	nil		3		(7 m)
20	Selvam	34/M	15221	L1 burst #	paraplegia	22.3.08	Post.stabilisation + pedicle screws	LD62, 63	LR 41	nil		3		(7 m)